ethylamine. The mixture was heated to the boil for 10 hr and then the ethanol and the excess of diethylamine were distilled off. The residue was dissolved in water and acidified. The neutral reaction products were extracted with ether and the aqueous solution was saturated with sodium carbonate. The organic bases that separated out were extracted with benzene, giving 0.25 g (0.7 mM) of **VIII** in the form of crystals deliquescing in the air; after washing with petroleum ether, mp 114–124° C. Found, %: N 14.19. Calculated for $C_{21}H_{34}N_4O_2$, %: N 14.97. **Dihydrochloride of VIII,** crystals rapidly deliquescing in the air. Found, %: Cl 16.22, 16.11. Calculated for $C_{21}H_{34}N_4O_2$, %: Cl 15.84. **Dipicrate of VIII,** mp 238–239° C (from ethanol). Found, %: N 16.31, 15.04. Calculated for $C_{21}H_{34}N_4O_2 \cdot 2C_6H_3(NO_2)_3OH$, %: N 16.82.

N-(1,2,5-Trimethylpiperid-4-yl)sulfanilamide. With cooling, 11.4 g (0.048 mole) of p-acetamidobenzenesulfonyl chloride was added in portions to 5.35 g (0.038 mole) of **I** in 20 ml of pyridine. The reaction was accompanied by pronounced heating and resinification. The mixture was diluted with water and the oil that floated to the top was extracted with benzene. The benzene was distilled off and the residue was treated with 100 ml of 6% caustic soda solution and heated at 100° C for 1.5 hr. Then the solution was acidified and the neutral reaction products were extracted with ether. The aqueous solution was treated with sodium carbonate and ether. The ethereal extract yielded 1.73 g (0.006 mole) of **IX** in the form of white crystals with mp 191–193° C (from acetone). Found, %: N 14.09, 13.98. Calculated for $C_{14}H_{23}N_3O_2S$, %: N 14.14.

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SOME METHYL AND BROMO DERIVATIVES OF 9-AMINO-6-NITROACRIDINE

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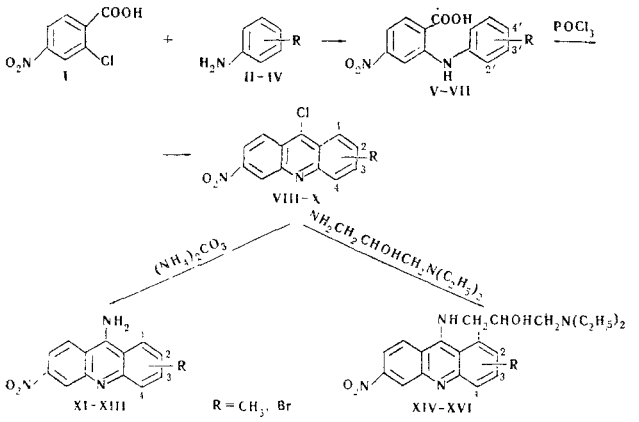
2-Methyl, 4-methyl, and 2-bromo derivatives of 9-amino-6-nitroacridine and of 9-(γ-diethylamino-β-hydroxypropylamino)-6-nitroacridine, and a number of intermediates in their synthesis, have been obtained.

It is known that alkoxy-substituted 9-amino-6-nitroacridines possess antimicrobial activity [1, 2]. At the same time, derivatives of 9-amino-6-nitroacridine containing other substituents have been studied inadequately. It appeared of interest to synthesize for biological tests some of its methyl and bromo derivatives. The synthesis was carried out in the following way:



The diphenylamine-2-carboxylic acids (V–VII) were obtained by the Ullman reaction from 2-chloro-4-nitrobenzoic acid (I) and the appropriate arylamines (o- and p-toluenes and p-bromoaniline) (II–IV). The acids **V–VII** were cyclized by treatment with phosphorus oxychloride in chloroform into the 9-chloro-6-nitroacridine derivatives (XI–XIII) or 9-(γ-diethylamino-β-hydroxypropylamino)-6-nitroacridines XIV–XVI.

Compounds V–XVI (see table) have been obtained for the first time, with the exception of 4'-methyl-5-nitrodiphenylamine-2-carboxylic acid [3]. The 2-methyl, 4-methyl-, and 2-bromo derivatives of 9-(γ-diethylamino-β-hydroxypropylamino)-6-nitroacridine (**XIV–XVI**) were isolated in the form of the dihydrochlorides, which are readily soluble in water. According to preliminary results, their antibacterial activity is higher than that of the corresponding methoxy derivatives [2]. The biological tests were carried out by I. Yu. Kholupyak under the direction of O. V. Chuiko.

EXPERIMENTAL

Diphenylamine-2-carboxylic acids (V–VII). A mixture of 0.15 mole of 2-chloro-4-nitrobenzoic acid, 0.3 mole of the required arylamine (o-toluidine, p-toluidine, or p-bromoaniline), 30 g of potassium carbonate, and 1 g of copper powder was heated in 150 ml of

Characteristics of the Compounds Obtained

Compound	Name	Mp*, °C	External form	λ_{max}**, nm	log ε	Empirical formula	N, % found	N, % calculated	Yield, %
1	2	3	4	5	6	7	8	9	10
V	2'-Methyl-5-nitrodiphenylamine-2-carboxylic acid	234—235	Red rhombs	234 278 420	4.11 4.32 3.47	$C_{14}H_{12}N_2O_4$	10.41 10.36	10.29	59
VI	4'-Methyl-5-nitrodiphenylamine-2-carboxylic acid	222—223***	Orange needles	237 282 425	3.98 4.28 3.39	—	—	—	80
VII	4'-Bromo-5-nitrodiphenylamino-2-carboxylic acid	248—249	Red plates	238 295 418	4.11 4.44 3.57	$C_{13}H_9BrN_2O_4$	8.52 8.59	8.31	51
VIII	1-Chloro-2-methyl-6-nitroacridine	199—200	Yellow needles	242 299 357 373	4.88 4.69 4.02 4.13	$C_{14}H_9ClN_2O_2$	10.33 10.49	10.28	92
IX	9-Chloro-4-methyl-6-nitroacridine	187—188	Yellow needles	242 297 351 368 397	4.55 4.33 3.66 3,65 3,51	$C_{14}H_9ClN_2O_2$	10.20 10.51	10.28	94
X	2-Bromo-9-chloro-6-nitroacridine	236—237	Golden needles	256 290 356 375	4,58 4.42 3.81 3.92	$C_{13}H_6BrClN_2O_2$	8.49 8.36	8.30	85
XI	9-Amino-2-methyl-6-nitroacridine	287—288	Kp Red plates	246 283 320 (364)	4.45 4.46 4.23 3.46	$C_{14}H_{11}N_3O_2$	16.81 16.68	16.60	93

1	2	3	4	5	6	7	8	9	10
				384 450	3.59 3.60				
XII	9-Amino-4-methyl-6-nitroacridine	238—239	Dark red needles	244 282 321 (362) 382 455	4.51 4.51 4.20 3.54 3.64 3.63	$C_{14}H_{11}N_3O_2$	16.72 16.79	16.60	90
XIII	9-Amino-2-bromo-6-nitroacridine	332—333	Dark red prisms	234 254 285 320 (366) 385 452	4.37 4.39 4.61 4.18 3.45 3.59 3.67	$C_{13}H_8BrN_3O_2$	13.17 13.44	13.21	88
XIV	9-(γ-Diethylamino-β-hydroxypropylamino)-2-methyl-6-nitroacridine dihydrochloride	185—186	Yellow plates	249 281 315 (357) 445	4.36 4.30 4.08 3.56 3.74	$C_{21}H_{26}N_4O_3 \cdot 2HCl \cdot H_2O$	12.15 12.00	11.84	85
XV	9-(γ-Diethylamino-β-hydroxypropylamino)-4-methyl-6-nitroacridine dihydrochloride	195—197	Dark yellow needles	246 280 313 (355) 440	4.40 4.41 4.07 3.38 3.79	$C_{21}H_{26}N_4O_3 \cdot 2HCl \cdot H_2O$	11.65 11.72	11.84	79
XVI	2-Bromo-9-(γ-diethylamino-β-hydroxypropylamino)-6-nitroacridine	217 (decomp.)	Brown prisms	257 283 (322) (372) 443	4.38 4.45 4.02 3.66 3.74	$C_{20}H_{23}BrN_4O_3 \cdot 2HCl \cdot H_2O$	10.62 10.59	10.41	82

*Solvents for the crystallization of compounds V and VII) glacial acetic acid; VI) aqueous ethanol; VIII–X) benzene; XI and XII) ethanol; XIII) aqueous dimethylformamide; XIV–XVI) absolute ethanol + ether.

**The UV spectra were taken in ethanolic solutions on an SF-4 spectrophotometer. The approximate values for the inflections of the bands are shown in brackets.

***According to the literature [3], mp 221°C.

n-amyl alcohol* at 160° C for 5 hr. The alcohol and the excess of amines were distilled off with steam and the solution was boiled with carbon, filtered, and brought to neutrality with concentrated HCl. The precipitate was separated off, washed with water, dried, and crystallized.

9-Chloroacridines (VIII–X). A mixture of 0.02 mole of the appropriate diphenylamine-2-carboxylic acid (**V–VII**), 5 ml of phosphorus oxychloride, and 15 ml of chloroform was heated in the water bath until dissolution was complete (2–6 hr) and then for another 30 min. The chloroform was distilled off in vacuum and the residue was poured into a mixture of ice and ammonia, after which the precipitate was separated off, washed with water, and dried in vacuum over caustic potash.

9-Aminoacridines (XI–XIII). With stirring, 1 g of the appropriate 9-chloroacridine **VIII–X** was dissolved in 3 g of phenol at 70° C, and 0.5 g of finely-ground ammonium carbonate was added in portions. Stirring was then continued at 120° C for 1 hr. The mixture was cooled and treated with 10% caustic soda, and the precipitate was separated off, washed with water, and extracted with boiling 5% acetic acid. The acetic acid filtrate was made alkaline with 10% NaOH, and the precipitate was filtered off, washed with water, dried and crystallized.

Dihydrochlorides of the 2-methyl, 4-methyl, and 2-bromo derivatives of 9-(γ-dimethylamino-β-hydroxypropylamino)-6-nitroacridine (XIV–XVI). With stirring, 5 mM of the appropriate 9-chloroacridine **VIII–X** was dissolved in 6 g of phenol at 70° C, and 6 mM of γ-diethylamino-β-hydroxypropylamine was added dropwise. The temperature was raised to 90–95° C and the mixture was stirred for another 2 hr. Then it was cooled, dissolved in absolute ethanol, and treated with ethanolic HCl solution until the reaction to Congo Red was acid and then with dry ether. The solvent was decanted off and the oil that had separated was washed with ether and dissolved in water. The aqueous solution was made alkaline with ammonia, and the precipitate was separated off and dried in vacuum over caustic potash. The dry substance (one of the bases **XIV–XVI**) was dissolved in absolute ethanol and the solution was made alkaline with ethanolic HCl and diluted with dry ether. The precipitate was separated off, washed with ether, dried in vacuum, and crystallized.

*In the preparation of 4'-bromo-5-nitrodiphenylamine-2-carboxylic acid (**VII**), n-hexanol was used.

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